UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,806	10/11/2005	Bernhard Gleich	DE 030116	5535

24737 7590 11/23/2010

PHILIPS INTELLECTUAL PROPERTY & STANDARDS
P.O. BOX 3001
BRIARCLIFF MANOR, NY 10510

EXAMINER	
DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
11/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,806	GLEICH, BERNHARD	
	Examiner	Art Unit	
	ERIC S. DEJONG	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/12/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-17,19,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-17,19,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

In view of the Appeal Brief filed on 07/12/2010, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim 4, 18, and 20-40 are cancelled. Claims 1-3, 5-17,19, 41, and 42 are pending and currently under examination.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3, 5-17,19, 41, and 42 under 35 USC 103(a) as being unpatentable over either of Heldmann et al. or Wasterby et al. in view of Zakharov et al. (Physical Review E, 2000) is withdrawn in view of the new grounds of rejection set forth below.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5-14-17,19, 41, and 42 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. This rejection is newly applied.

The instant claims are drawn to a method of determining physical, chemical and/or biological state variables in an examination area of an examination object by determining a change in a spatial distribution of magnetic particles in an examination area. The recited steps of the claimed process are directed to a general application of Nuclear Magnetic Resonance (NMR) spectroscopic procedures that, when practiced, result in the evaluation of signals to obtain information about "physical, chemical, and/or biological state variables" (see for example claims 1, lines 23-28). The scope of the

properties covered within the recited limitation "physical, chemical, and/or biological state variables" is essentially unbounded because any characteristic property of an "examination object" in an NMR experiment will fall into one of the generic categories of being a physical, chemical, and/or biological state variable.

However, the instant claims do not recite any particular improvement or resultant characteristic that is imparted to the "physical, chemical, and/or biological state variables" that would be used to yield any new and useful information. Rather, the practice of the instantly claimed process is directed only to obtaining a previously unmeasured property (a "physical, chemical, and/or biological state variable") of an unspecified sample (an "examination object") by means of a generalized NMR spectroscopic procedure.

The Court of Patent and Appeals has stated:

> "Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." A 'use' to do further research is not considered a utility which provides an "immediate benefit" to the public.
> Examples of situations requiring further research to identify or reasonably confirm a "real world" context of use, and which do not have utility under 35 USC 101, as set forth in MPEP 2107.01.1, include:
> (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved', and
> (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility.

The instant claims encompass a process of basic research drawn to studying properties (a "physical, chemical, and/or biological state variable") of a protein structure and as such do not result in an "immediate benefit" to the public. As noted in the utility guidelines (see Federal Register, December 21, 1999, Vol. 64, No. 244), basic research

on a product to identify properties is an insubstantial utility. Therefore, the instant claims do not have a substantial utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-17,19, 41, and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Collin et al. (Nucleic Acids Research (2000) in light of Evens (Biomolecular NMR Spectroscopy, Oxford Press, 1995) and Piotto et al. (Journal of Biomolecular NMR, 1992). This rejection is newly applied.

The recited process comprises the steps of introducing into an examination area magnetic particles in a first state or a second state, wherein at least some of the magnetic particles that are to be examined are agglomerated and/or coupled to one another in the first state and deagglomerated and/or decoupled in the second state.

Collin et al. teaches the application of NMR experiments applied to samples of isotopically labeled DNA and RNA at 1mM concentrations recorded on a Bruker DRX-600 spectrometer and a Bruker DRX-800 spectrometer equipped with triple resonance, three-axis gradient probes. See Collin et al. page 3386, col. 2, line 35 through page 3387, col. 1., line 5.

Evans et al. is relied upon for support that the natural abundance of 1H nucleic and isotopically enriched 15N in the 1mM concentration samples of isotopically labeled DNA and RNA, as taught by Collin et al., are magnetic particles. Specifically 1H and 15N nuclei are have a nuclear magnetic “spin” of ½ and can exist in one of two quantum states, denoted as "up" and "down", with respect to large external magnetic field. See Evans et al., section 1.1 Basic Theory of NMR, pages 5-9 and Table 1.2.

The recited process further comprises generating a magnetic field having a field strength with a gradient profile, such that there is a produced in the examination area two part areas including a first part-area having low magnetic field and a second part area having a higher magnetic field strength. The recited process further comprises changing spatial positions of the two part areas or changing the magnetic field strength in the first part area to cause the change in the spatial distribution of magnetic particles so that magnetization of the particles is locally changed.

Collin et al. teaches the use of three-axis gradient probes and the application of NMR experiments involving the use of transverse gradients. See Collin et al., page 3386, col. 2, line 35 through page 3387, col. 1., line 32.

Piotto et al. is further relied upon for support that the WATERGATE pulse program procedure as applied and taught in Collin et al. comprises the application of magnetic field gradient pulse applied across the entirety of a sample under investigation. See Piotto et al., Abstract, page 662 in it’s entirety, and Figure 1. The application of a field-gradient pulse introducing a magnetic field across the sample

varies as a function of sample position, and therefore meets the recited limitation of a first and second area of differing magnetic field intensity.

The recited process further comprises detecting signals that depend on the magnetization in the examination area that is influenced by the changing act. The recited process further comprises evaluating signals so as to obtain information about the change in the spatial distribution of the magnetic particles and about physical, chemical, and/or biological state variables that include at least one substance concentration, temperature, pressure, viscosity, and pH, to which the change is correlated.

Collin et al. teaches the use of a 2D 1H-15N HSQC experiment that involves detecting the magnetization properties of a concentrated nucleic acid sample in the form of a Free Induction Decay (FID) (see also Evans et al., page 11 and Figure 1.12). See Collin et al., page 3387, col. 1, lines 13-32. Collin et al. further teaches the evaluation of the collected data. See Collin et al., page 3387, col. 1, lines 20 and 21. Figure 1 is further relied upon to demonstrate that the information determined from the described NMR experiments involves and is directly correlated to sample concentration and pH dependencies.

Dependent claim 2 further recites the detecting act includes detecting change of the magnetic particles from the first state to the second state including deagglomeration and/or decoupling of coupled individual magnetic particles and/or detecting increased distance between magnetic particles.

Evans et al. is relied upon for support that the 1H-15N HSQC NMR experiment of Collin et al. is selective for determining those 1H and 15N that are coupled to one another through covalent bonds that exist in a given molecule and is selective against those 1H and 15N that are not coupled and, therefore, do not share a covalent bond. See Evans et al., Sect. 2.1.6: Heteronuclear correlation spectroscopy, pages 66 through 71.

Dependent claim 3 further recites the detecting includes detecting passage of the magnetic particles between the first state and second state, the passage being due to. at least one of heat, radiation, acid, base, electrical or magnetic fields, ultrasounds, and/or and enzyme.

Evans et al. is relied upon for support that the passage of magnetization between particles in a first and second state, as taught by Collin et al., is inherently an electomagnetic phenomenon. See Evans et al., Sect. 2.1.6: Heteronuclear correlation spectroscopy, pages 66 through 71.

Dependent claim 5 recites that the act of spatially delimiting the agglomerated magnetic particles in a medium which can be physically, chemically, and/or biologically modified, dissolved, and/or modified.

Figure 1 of Collin et al. is relied for demonstrating that the aqueous compositions under analysis can be modified to contain different concentrations of both DNA and RNA samples as well as to contain different buffering conditions and agents.

Dependent claim 9 recites that the act of saturating the magnetic particles by act of application of an external magnetic field having a strength of about 100mT or less.

Piotto et al., Figure 2 is relied upon for support that the WATERGATE NMR procedure used by Collin et al. involves the application of 17.5 kHz non-selective and 165 Hz selective RF, which correlates to a field strength of the corresponding electromagnetic pulse to less than 100mTesla.

Dependent claims 10 and 12 recite the magnetic particles are monodomain or multidomain and further comprising the act of reversing magnetization of the multidomain or monodomain particles by Neel's rotation and Brown's rotation. Dependent claim 11 and 12 recites wherein the magnetic particles are hard-magnetic or soft-magnetic particles.

Table 1.2 of Evans et al is relied upon for support that 1H ad 15N of Collin et al. are inherently dipolar spin ½ particles whose quantized spin state can be influence by Neel's and Brown's rotation.

Dependent claim 13 recites binding magnetic particles to functional binding units including a functional group, a DNA sequence, and RNA sequence, and an aptamer, and introducing at least one compound which has complementary binding units and an aptamer sequence that interact in a binding manner with at least one functional binding unit of the magnetic particles.

Collin et al. presents the results of the above described NMR procedures and analysis on an RNA-DNA aptamer complex consisting of a 18 nt RNA hairpin and a 20 nt DNA aptamer. See Collin et al., Abstract.

Dependent claim 41 recites the act of changing magnetic fields includes changes the magnetic field strength temporally in a first frequency band and the detecting act

includes detecting the signal in a second frequency band and the second frequency band including harmonics of signals in the first frequency band. Dependent claim 42 recites the act of generating the magnetic field further includes the act of first and second magnetic fields which change at different rates and with different amplitudes, wherein the first magnetic field changes slowly in time and the second magnetic field changes rapidly in time terms and with lower amplitude relative to the first magnetic field.

Evans et al. is relied upon for support that the use of a low power, saturating RF frequency pulse applied on the solvent resonance frequency during data collection, as taught in the method of Collin et al., inherently suppresses unwanted wanted solvent signature. See Evans et al., Sect. 2.1.8 Solvent Suppression, pages 75-76.

Response to Arguments

Applicant's arguments with respect to claims 1-3, 5-14-17,19, 41, and 42 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ERIC S. DEJONG/
Primary Examiner, Art Unit 1631